

analogs is associated with a tag that identifies a particular nucleotide analog carried by the linker, wherein interaction of the tag associated with the polymerizing agent with the tag associated with the nucleotide analog induces emission of the characteristic signal that indicates pairing of the nucleotide analog on the linker with its complementary nucleotide in the target nucleic acid molecule.

12. The probe of claim **11**, wherein the tag associated with the polymerizing agent forms a donor-acceptor pair with the tag associated with each nucleotide analog, whereby interaction of the donor-acceptor pair stimulates emission of the characteristic signal.

13-14. (canceled)

15. The probe of claim **11**, wherein each of the tags that identifies a particular nucleotide analog carried by the linker, comprises one or more fluorophores that emits a unique emission signal.

16. The probe of claim **1**, wherein the one or more molecular linkers comprise four molecular linkers, each of which carries a different nucleotide analog capable of reversibly binding to the template strand of the target nucleic acid molecule without being detached from the linker, and an acceptor tag associated with each nucleotide analog wherein the acceptor tag identifies the particular nucleotide analog carried by the linker, and the polymerizing agent is associated with a donor tag, wherein reversible binding of the nucleotide analog to the target nucleic acid molecule brings the donor and acceptor tag into sufficient proximity to induce emission of a characteristic signal of the acceptor tag that indicates the identity of the nucleotide analog carried by the linker.

17. The probe of claim **1**, wherein the one or more molecular linkers are spaced around the polymerizing agent a sufficient distance to inhibit entanglement of the molecular linkers, and the molecular linkers are of sufficient length to reach the active site of the polymerizing agent.

18-20. (canceled)

21. The probe of claim **1**, wherein at least a portion of the molecular linker is of a sufficient rigidity to reduce interaction of the polymerizing agent and the nucleotide analog in the absence of the target nucleic acid molecule.

22-23. (canceled)

24. The probe of claim **1**, wherein the molecular linker comprises a double-stranded DNA (dsDNA) of at least 10 nucleotides.

25. (canceled)

26. The probe of claim **1**, wherein the molecular linker comprises polyethylene glycol (PEG).

27-30. (canceled)

31. The probe of claim **1** where the polymerizing agent comprises a DNA polymerase, RNA polymerase, ribosome, or reverse transcriptase.

32-35. (canceled)

36. A polymerizing agent comprising:

an active site capable of binding to a target nucleic acid molecule and promoting synthesis of a complementary nucleic acid molecule that elongates as complementary nucleotides are incorporated into the complementary nucleic acid molecule;

one or more molecular linkers spaced apart on the polymerizing agent to inhibit entanglement, wherein each linker carries a different nonhydrolyzable nucleotide analog that is capable of reversibly binding to the template strand of a nucleic acid molecule, without being

detached from the linker, by specifically binding with a complementary nucleotide in the target nucleic acid molecule;

a tag associated with each nonhydrolyzable nucleotide analog that identifies the nonhydrolyzable nucleotide analog carried by the linker that is capable of reversibly binding to the template strand of a nucleic acid molecule; and

a tag associated with the polymerase that interacts with the tag associated with the nonhydrolyzable nucleotide analog to emit a characteristic signal that identifies the nonhydrolyzable nucleotide analog carried by the linker.

37. A method of determining a nucleic acid sequence of a target nucleic acid molecule, comprising:

exposing the target nucleic acid molecule to the probe of claim **1** in the presence of an oligonucleotide primer and a mixture of hydrolyzable nucleotides that are capable of being incorporated into an elongating nucleic acid molecule by hybridizing with a complementary nucleotide in the target nucleic acid molecule, and replacing the nucleotide analog that reversibly binds to the template nucleic acid molecule;

detecting emission of a sequence of signals comprising emission of a plurality of the characteristic signals that indicates pairing of the nucleotide analog on the molecular linker with its complementary nucleotide.

38. The method of claim **37**, wherein the polymerizing agent is associated with a tag, and each of the chemical moieties is also associated with a tag that identifies a particular nucleotide analog carried by the linker, wherein interaction of the tag associated with the polymerizing agent with the tag associated with the nucleotide analog induces emission of the characteristic signal that indicates pairing of the nucleotide analog on the linker with its complementary nucleotide.

39. The method of claim **38**, wherein the tag associated with the polymerizing agent comprises a donor fluorophore and the tag that identifies a particular nucleotide analog comprises one or more acceptor fluorophores, wherein interaction of the polymerizing agent and the nucleotide analog that specifically binds to the complementary nucleotide in the target nucleic acid molecule brings the acceptor fluorophore into a proximity with a donor fluorophore to permit excitation of the acceptor fluorophore by the donor fluorophore.

40. The method of claim **39**, wherein detecting the signal comprises detecting a fluorescent signal emitted from the acceptor fluorophore or comprises detecting a reduction in fluorescent signal emitted from the donor fluorophore.

41. The method of claim **37**, wherein the emission of a sequence of signals is converted into a nucleic acid sequence.

42. (canceled)

43. The method of claim **39**, further comprising exciting the donor fluorophore to emit a signal which excites the one or more acceptor fluorophores to emit the characteristic signal that indicates pairing of the nucleotide analog on the linker with its complementary nucleotide.

44-50. (canceled)

51. The method of claim **37**, wherein the probe is fixed to a substrate.

52-53. (canceled)

54. The method of claim **37**, wherein the target nucleic acid molecule or the oligonucleotide primer is fixed to a substrate.

55. The method of claim **37**, wherein the method comprises performing a plurality of sequencing reactions substantially